

### ABSTRACT

The present invention relates to the use of tumor suppressor genes in combination with a DNA damaging agent or factor for use in killing cells, and in particular cancerous cells. A tumor suppressor gene, p53, was delivered via a recombinant adenovirus-mediated gene transfer both *in vitro* and *in vivo*, in combination with a chemotherapeutic agent. Treated cells underwent apoptosis with specific DNA fragmentation. Direct injection of the p53-adenovirus construct into tumors subcutaneously, followed by intraperitoneal administration of a DNA damaging agent, cisplatin, induced massive apoptotic destruction of the tumors. The invention also provides for the clinical application of a regimen combining gene replacement using replication-deficient wild-type p53 adenovirus and DNA-damaging drugs for treatment of human cancer.